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EXAMINER

SOUW, BERNARD E

ART UNIT

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/536,908	<b>Applicant(s)</b> ASOGAWA ET AL.	
	<b>Examiner</b> BERNARD E. SOUW	<b>Art Unit</b> 2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 8/12/2008 (Appeal Brief).
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 10-12, 16, 21-26, 30, 31 and 34-39 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5-7, 10, 36 and 37 is/are allowed.
- 6) ☒ Claim(s) 1-4, 16, 21-26, 30, 31, 34, 35, 38 and 39 is/are rejected.
- 7) ☒ Claim(s) 11 and 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 August 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                      |                                                                   |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____                                                          | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Reopening of Prosecution After Appeal Brief or Reply Brief***

1. In view of the Appeal Brief filed on 08/12/2008, PROSECUTION IS HEREBY REOPENED. Reason for reopening this prosecution is set forth below.

Except for some changes in the language of previous Final Rejection dated 11/16/2007, including elimination of one redundant prior art, all the rejections are held *prima facie* obvious for the same reason and over the same prior art of record.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

### ***Arguments/Remarks***

2. The Argument & Remarks filed on 08/12/2007 (Appeal Brief) in response to the Final Office Action dated 11/16/2007 has been entered. The present Office Action is made with all the suggested amendments being fully considered, but they are not considered persuasive.

No claim has been amended, cancelled, or added.

Claims 8, 9, 13-15, 17-20, 27-29, 32 and 33 have been previously cancelled.

Pending in this Office Action are claims 1-7, 10-12, 16, 21-26, 30, 31 and 34-39.

3. Claims 21, 22 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (USPAT 6,696,022) in view of Carle et al. (USPAT 5,167,790).

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► As per claim 21, Chan et al. disclose an electrophoretic separation method using a separation apparatus shown in Fig.1 (xix or xx), Fig.2 (a-d, h, k, l, m), Figs.12, 14, 15 and 20, as recited in Col.19/II.45-56 and Col.20/II.37-65, comprising:

(a) a channel, as shown, e.g., in Fig. 2(b), through which a sample containing components-to-be-separated moves, as recited in Col.30/II.16-20;

(b) a plurality of compartments provided to the channel (separated by obstacles or posts represented by dots in Fig.2(b)), as recited in Col.19/II.49-53; and

(c) an external force imposing unit (not shown, but recited in Col.31/II.32-35), imposing external (electrophoretic) force to a sample containing components-to-be-separated so as to allow the sample to move through said channel, wherein said external force imposing unit has a function of executing a first external force imposing pattern by which the external force is imposed to the sample in the forward direction along the channel, as recited in Col.30/II.16-20 and Col.31/II.3-50, esp. II.29-50.

However, Chan et al. failed to teach a second external force imposing pattern in the direction opposite to the forward direction along the same channel. Carle et al. teach a reverse field electrophoresis method, in which the sample containing components-to-be-separated is exposed to an external force pointing in the direction opposite to the forward direction along the channel (i.e., field-inversion electrophoresis), as recited in Col.3/II.53-60 and Col.10/II.66-68, to thereby "*fractionate*" the components-to-be-separated into spatially separated bands 1-8, contained in lanes A-E shown in Fig.4), as recited in Col.11/II.6-39, the word "*to fractionate*" being understood in the art as "*to spatially separate*", not as "*to break the molecular chain apart*".

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Chan's method by adding the step of imposing a second external force in the direction opposite to the forward direction along the channel, i.e., applying Carle's field-inversion electrophoresis, in order to enhance the spatial separation of the sample into separated compartments, wherein Carle's separation bands 1-8 correspond to Chan's compartments (separated by dots in Fig.2(b)).

One of ordinary skill in the art would have been motivated to apply Carle's field-inversion electrophoresis, in order to enhance spatial separation by successive application of force and thereby achieve high throughput, as taught by Chan et al. in Col.15/II.61-64.

► Regarding claim 22, the migration ranges of the fractionated sample are shown by Carle et al. as bands 1-8 shown in Fig.4, as recited in Col.11/II.6-39.

► As per claim 34, Carle's system comprises an external force switching control unit 13 shown in Fig.1 and 3, as recited in Col.9/II.11-14.

4. Claims 16, 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Carle et al., and further in view of Shimoide et al. (USPAT 7,105,354)).

Chan et al. as modified by Carle et al. show all the limitations of claim 16, more specifically regarding field-inversion electrophoresis, as previously applied to independent claim 21, except the additional limitations of (a) a channel having a main channel and sub-channels formed as being branched out from said main channel; and

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(b) a main channel having one end where a sample introduction port is provided and the other end placed downstream of said one end (i.e., the sample introduction port).

Regarding limitation (b), one of ordinary skill in the art understands that Chan's embodiment shown in Fig.12, or more clearly Fig.15, is provided with a sample introduction port, and the other end is placed downstream of the sample introduction port, wherein the downstream (or flow) direction is unambiguously indicated by an arrow and also labeled as such.

Regarding limitation (a) the embodiment(s) above is to be combined with Chan's other embodiments which are furnished with a main (central) channel and sub- (or side) channels formed as being branched out from said main channel, as shown in Fig.1(vii), 1(viii), (ix), (x), (xi), as recited in Col.20/ll.7-17, and Fig.2(c)/middle, 2(f), 2(j), 2(m)/top, as recited in Col.8/ll.28-30 + 65-67.

However, Chan et al. do not expressly recite in which direction the sample is moving, i.e., whether from the branches merging into the main channel, or from the main channel diverting into the sub-channels. Shimoide et al. teach a particular embodiment in which the sample is diverted from the main channel into the sub-channels, as recited in Col.26/ll.38-40.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Chan's apparatus having a plurality of sub-channels formed by Carle's field-inversion electrophoresis, in order to enhance the separation effect in Chan's apparatus.

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It would have been obvious to one skilled in the art to fractionate the sample into the sub-channels, as taught by Shimoide et al., and to detect, extract or collect the fractionated components with higher resolution, as taught by Chan et al.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Chan's channel structure with Shimoide's sub-channels branched out from a main channel, since such a branching structure allows sample injection from a single inlet port, and yet multiple extractions of components from a plurality of collection ports, as taught by Shimoide et al.

One of ordinary skill in the art would have been motivated to combine Chan's branching structure with Carle's field-inversion electrophoresis, in order to achieve high throughput of the separation (or selection, or screening) process, as taught by Chan et al. in Col.15/II.61-64.

Regarding the last limitations of claim 16, i.e., "*..... so that a portion of said components-to-be-separated is moved to the downstream of the connecting position of said main channel and one of said sub channels in said main channel and subsequently imposing a second external imposing pattern having a different imposing direction .....*," this limitation is understood by those of ordinary skill in the art as imposing an external field in the downstream direction so as to move the components **pass a branching point** to a sub channel (moved to the downstream of the connecting position of said main channel and one of said sub channels), then followed by field-inversion electrophoresis.

This specific step is obvious to one of ordinary skill in the art, even without auxiliary teaching, but solely by following Carle's teaching of field-inversion electrophoresis in combination with Chan's compartments as modified by Shimoide's sub channel. Upon repeating the periodic reversals of the electrophoretic field for a sufficient number of times, such that some separated components would have passed beyond certain branching point(s), one of ordinary skill in the art would find some of the components already entered the sub channel by the time when the field is reversed (of course, one of ordinary skill in the art --again without auxiliary teaching-- would apply a reverse voltage on the other end of the branch, since otherwise the field-inversion method would not be properly carried out). What remains to be done is merely an optimization to enhance the effect already observed, which is not patentable for involving only routine skill in the art.

► Claim 30 is a method claim reciting the same limitations as claim 16. Therefore, claim 30 is also rejected along with claim 16 over the same prior art references, including the pertinent reasons and motivations to combine.

► Regarding claim 31, the duration of Carle's external force in the first step (of claim 30), i.e., in the forward direction, is kept constant at 3 sec (while being repeated for 12 hours long), as recited in Col.10/ll.66-68.

5. Claims 1-4, 23-26, 38 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Carle et al. and Anderson et al. (USPGPub 2001/0036672).

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► Chan et al. as modified by Carle et al. show all the limitations of claim 1, as previously applied to the other, previously rejected, independent claims 16 and 21, except the recitation of one, or two, or more check valves disposed in said channel, partitioning the plurality of compartments and suppressing back flow of said components-to-be-separated. This limitation is rendered obvious by Anderson et al.

Anderson et al. disclose a fluid treatment device shown in Fig.3 that also includes sample separation channel (sect.[0011]/ll.3-5), in which electrophoresis is used to separate/analyze the sample, as recited in sect.[0083]/ll.1-6 and [0084]/ll.1-11, particularly using the embodiment shown in Fig.3, which includes compartments 202, 206, 210, 214 and 218, connected to fluid channels 208, 212 and 216, respectively, as recited in sect.[0111]/ll.1-6. Particularly regarding claim 1, a check valve is used in Anderson's separation apparatus, as recited in sect.[0112]/line 9, more particularly in sect.[0133]/ll.1-6 from bottom, and further, in sect.[0166]/ll.1-10. Anderson's check valve, as recited in sect.[0033], is functionally the same as Chan's obstacles, or posts.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify Chan's apparatus with Anderson's check valves, since the check valve remains effective for the fractionated components as the only part that still moves within the channels, thus preventing the latter from leaking-back and mixing-up with the other fractionated sample(s) in the adjacent compartment(s).

One of ordinary skill in the art would have been motivated to modify Chan's & Carle's apparatus with Anderson's check valves to separate Chan's compartments,

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since the check valves allows a clean separation of the fractionated samples with little chance of intermixture, thus enhancing the resolution of the device.

► Regarding claim 2, Chan's channels shown in Figs.1 (xxi), Figs. 2(a)(b)(c)(l),(m) extend in a straight form. Anderson's channels shown in Fig.3, 6A, and 6B are also straight in form. Thus, Chan's channel as modified by Anderson is also straight in form.

► Regarding claim 3, Anderson's check valve blocks a back flow of the fluid medium to an upstream side while moving it towards the downstream side of the channel, as expressly recited in sect.[0133]/II.1-8 from bottom. Carle's inverse field technique as modified from Chan et al. imposes the external force (field) periodically, i.e., repeatedly, as recited in Applicant's claim 3. The rest of the limitations of claim 3 are the same as those of claim 21, which have been previously rejected as being obvious over Carle et al. as modified by Chan et al. Therefore, claim 3 is also rejected over the same prior art, but now with Anderson et al. as an additional prior art just because of its dependency on claim 1.

► Regarding claim 4, the electrodes and the applied voltages are rendered obvious by Chan et al. in Col.3/II.32-35, whereas changing the direction of the voltage is rendered obvious by Carle's field-inversion electrophoresis, as already recited previously.

► Regarding claim 23, the repeated steps of applying the external force within one compartment towards downstream, and then reversed towards the upstream, is nothing else but field-inversion electrophoresis that has been previously rendered obvious by Carle et al., as recited in Col.3/II.53-68.

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► Regarding claims 24 and 25, the limitation that the duration of imposing external force is kept constant in every execution step of claim 23, i.e., in the forward as well as in the backward direction, is implicated by Carle et al. in Col.3/ll.64-66, wherein the external force in the forward direction is higher than the voltage applied in the reverse direction, in order to have a forward net migration of the samples, especially for molecules having very low differential mobility due to their very short conformation time relative to the reverse field interval or period, as taught by Carle et al. in col.5/ll.1-20 and col.6/ll.1-25.

► Regarding claim 26, the limitation that the duration of external force in the second step of claim 23 (upstream, in reverse direction) can be equal to, or longer than, in the first step (downstream, in forward direction) is inclusively implicated by Carle et al. in Col.3/ll.64-68, whereby it is self-obvious to simultaneously adjust the external force in the second step to be smaller than in the first step, in order to ensure a forward net migration of the sample.

► As per new claims 38 and 39, the two claim limitations are nothing else but a detailed description, how a flow blockage by Anderson's check valves works, so as to cause spatial separation of the components, wherein the recited "*suppressing portion*" is nothing else but the check valves, and the "*second external imposing pattern having a different imposing direction*" is nothing else but Carle's reverse electrophoresis field.

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6. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carle et al. in view of Chan et al. and Anderson et al. and further in view of Hancock et al. (USPAT 5,716,825).

Carle et al. as modified by Chan et al. and Anderson et al. show all the limitations of claim 35, as previously applied to the parent claim 1, except the recitation of a specific mass spectrometric system being coupled to the sample separation apparatus of claim 1.

Hancock et al. disclose a MALDI/TOF mass spectrometry (MS) system, as recited in Col.11/ll.9-16, the MS system comprising:

A pre-treatment (or pre-analysis) unit separating a biological sample depending on the molecular size or properties, as recited in Col.11/ll.9-16 (wherein a DNA obviously represents a biological sample, as recited in Col.1/ll.46-55), and subjecting said sample to a pre-treatment (preparation) for an enzyme digestion treatment, the sample preparation or pre-treatment expressly recited in Col.7/ll.66-67 and Col.8/ll.1-10, whereas the enzyme digestion treatment is expressly recited in Col.2/ll.9-14; a unit subjecting said sample pre-treated by said pre-treatment unit to the enzyme digestion treatment, as already recited in Col.2/ll.23-24; a drying unit drying the enzyme-digestion-treated sample, as recited in Col.10/ll.39-46; and a mass spectrometry unit subjecting the dried sample to mass spectrometry, as recited in Col.10/ll.59-63, wherein the term “*dried*” being expressly recited in line 61. The limitation that Hancock’s microchannel system including the pre-treatment unit comprises a miniaturized unit, is recited in Col.3/ll.1-20, more specifically as “*microchannel*” and “*chip*” in Col.4/ll.34-55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to couple Hancock's mass spectrometer system to the sample separation apparatus of Carle et al. as modified by Chan et al. and Anderson et al., in order to determine and/or identify not only the size, but also the mass and the molecular constituents of the fractionated sample.

One of ordinary skill in the art would have been motivated to modify the sample separation apparatus of Carle et al., Chan et al. and Anderson et al., particularly with Hancock's MALDI/TOF spectrometer, since the latter not only is capable of fragmentizing the fractionated sample, but is further equipped with a number of processes relating to enzyme digestion treatment and/or research, all those in the form of a tiny microchip that would allow automated and batch processing.

### **ALLOWANCE**

7. Claims 5-7, 10, 36 and 37 are allowed

### ***Reasons for Allowance***

8. The following is a statement of reasons for allowance:

► Independent claim 5 (amended) is allowed for reciting the limitation of "*imposing patterns having different imposing directions from each other to said components-to-be-separated so as to allow them to move through a channel*", wherein the first imposing pattern has a certain direction so that a portion of said components-to-be-separated is intercepted by one of the bent portions of the channel, and the subsequent (second)

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components-to-be-separated that has been previously intercepted by said one of said bent portions is now moved to the downstream next compartment.

► Claims 6, 7, 10, 36 and 37 are also allowed for their dependency, either directly or independently, on the previously allowed claim 5.

***Indication of Allowable Subject Matter***

9. Claims 11 and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Reasons for Indication of Allowable Subject Matter***

10. The following is a statement of reasons for the indication of allowable subject matter:

► Claim 11 is allowable for reciting the limitation that the length of a channel placed on the further downstream side has a larger length, which may result in equal migration times required by the fractionated components to move forward within each successive compartment. Whatever purpose Applicant has in mind, it is non-obvious to require larger lengths for channels placed further downstream. This is a unique design choice having a special purpose that underlines Applicant's invention not anticipated or rendered obvious by any prior art.

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► Claim 12 is allowable for reciting the limitation that a smaller external force is to be applied to a channel placed further downstream, which also may result in about the same migration time required by the fractionated components to move forward within each successive compartments (since the fractionated component further downstream moves forward at a higher migration velocity). Again, irrespective of whatever purpose Applicant has in mind, it is non-obvious to require a smaller external force to be applied to a channel placed further downstream. This is another unique design choice underlining Applicant's invention not anticipated or rendered obvious by any prior art.

### ***Final Rejection***

11. No new ground(s) of rejection is presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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***Communications***

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bernard E Souw, whose telephone number is 571 272 2482. The examiner can normally be reached on Monday thru Friday, 9:00 am to 5:00 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Kim can be reached on 571 272 2293. The central fax phone number for the organization where this application or proceeding is assigned is 571 273 8300 for regular communications as well as for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571 272 5993.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Bernard E Souw/  
Primary Examiner, Art Unit 2881

/ROBERT KIM/

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Supervisory Patent Examiner, Art Unit 2881